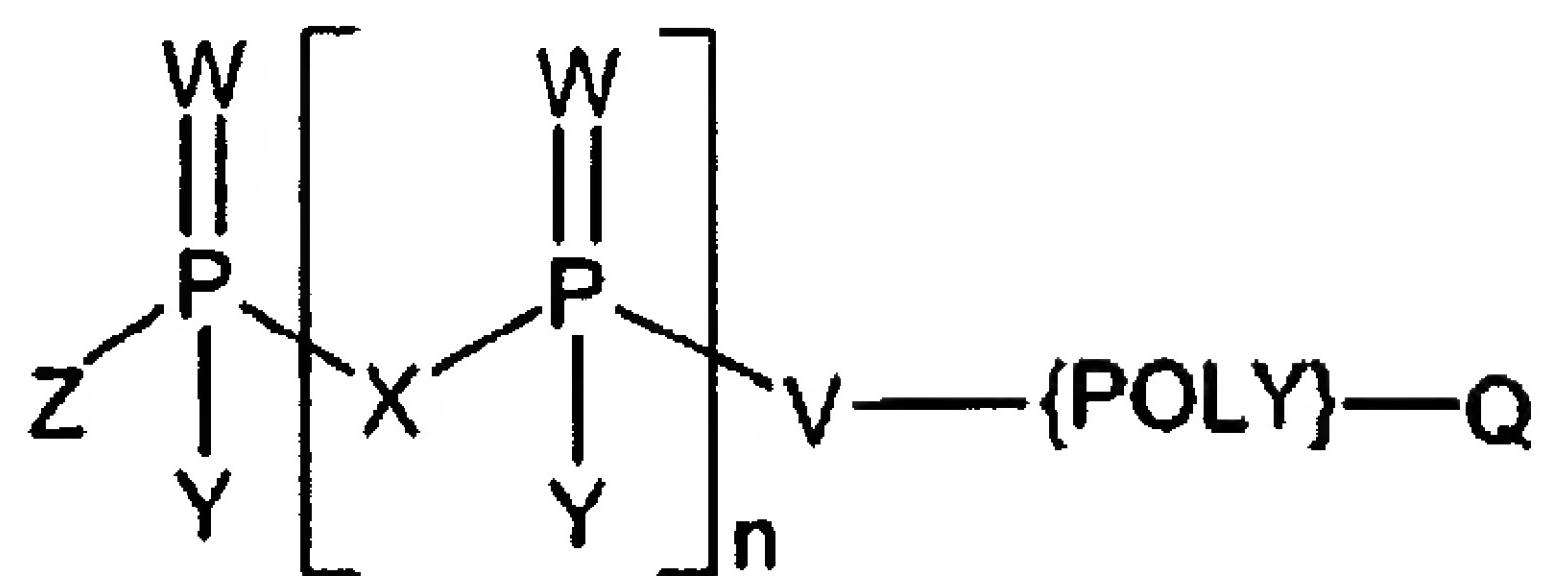


Claims

ALLOWED ~~FEES~~/ TJ

1. A PNA derivative of Formula I



Formula I

wherein

V is oxygen, sulfur, NR<sub>1</sub>, U-(CR<sub>3</sub>R<sub>4</sub>)<sub>U'</sub>-CH<sub>2</sub>-C(O)-NH, or U-(CH<sub>2</sub>CH<sub>2</sub>O)<sub>U'</sub>-C(O)-NH;

U is, independently of any other U, oxygen, sulfur, or NH;

U' is, independently of any other U', from 1 to 10;

W is, independently of any other W, oxygen, sulfur, or NR<sub>1</sub>;

Y is, independently of any other Y, hydroxyl, mercapto, oxyanion, thioate, or NR<sub>1</sub>R<sub>2</sub>,

R<sub>1</sub> and R<sub>2</sub> are, independently of each other, a radical consisting of hydrogen or C<sub>1</sub>-C<sub>6</sub>-alkyl;

R<sub>3</sub> and R<sub>4</sub> are, independently of each other, a radical consisting of hydrogen or a C<sub>1</sub>-C<sub>6</sub>-alkyl, or the radical of an amino acid side chain:

- X is, independently of any other X,
  - U-(C<sub>2</sub>-C<sub>22</sub>-alkanediyl)-U,
  - U-(CH<sub>2</sub>CH<sub>2</sub>-O)<sub>u'</sub>.
  - a bifunctional labeling group;
  - a bifunctional group for crosslinking with complementary nucleic acids,
  - a bifunctional group which promotes intracellular uptake, or
  - a bifunctional group which increases the binding affinity of the PNA derivative for a target nucleic acid;
- Z is hydroxyl,
  - mercapto,
  - oxyanion,
  - thioate,
  - NR<sub>1</sub>R<sub>2</sub>,
  - C<sub>1</sub>-C<sub>22</sub>-alkyl,
  - C<sub>1</sub>-C<sub>8</sub>-arylalkyl,
  - C<sub>1</sub>-C<sub>22</sub>-alkyl-U,
  - C<sub>1</sub>-C<sub>8</sub>-arylalkyl-U,
  - hydroxy-C<sub>1</sub>-C<sub>18</sub>-U,
  - aminoalkyl-U, arylalkyl-U or mercaptoalkyl-U,
  - a group of the formula R<sub>9</sub>(CH<sub>2</sub>CH<sub>2</sub>-O)<sub>m</sub>, wherein R<sub>9</sub> is hydroxyl, amino, or C<sub>1</sub>-C<sub>22</sub>-alkoxy, and m is from 1 to 100,
  - a monofunctional or bifunctional labeling group,
  - a monofunctional or bifunctional crosslinking group.

a monofunctional or bifunctional group which promotes intracellular uptake, or

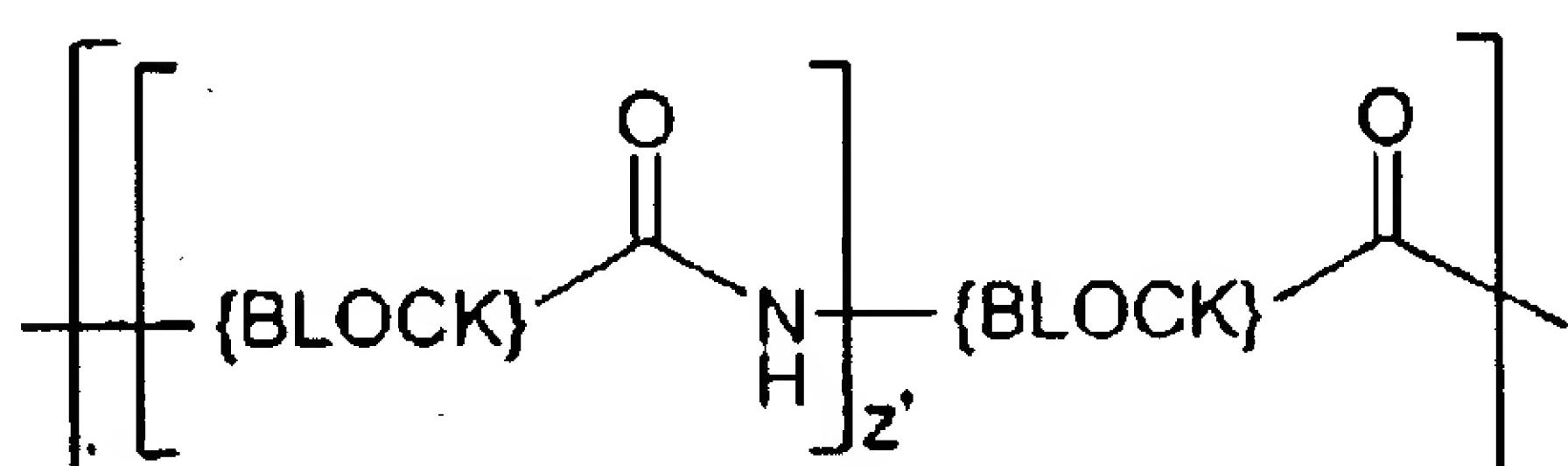
a monofunctional or bifunctional group which promotes the binding affinity of the PNA derivative for a target nucleic acid;

n is from 0 to 10;

Q is hydroxyl, amino,  $\text{NHR}_7$ ,  $\text{NR}_7\text{R}_8$ , an amino acid derivative, or a peptide radical,

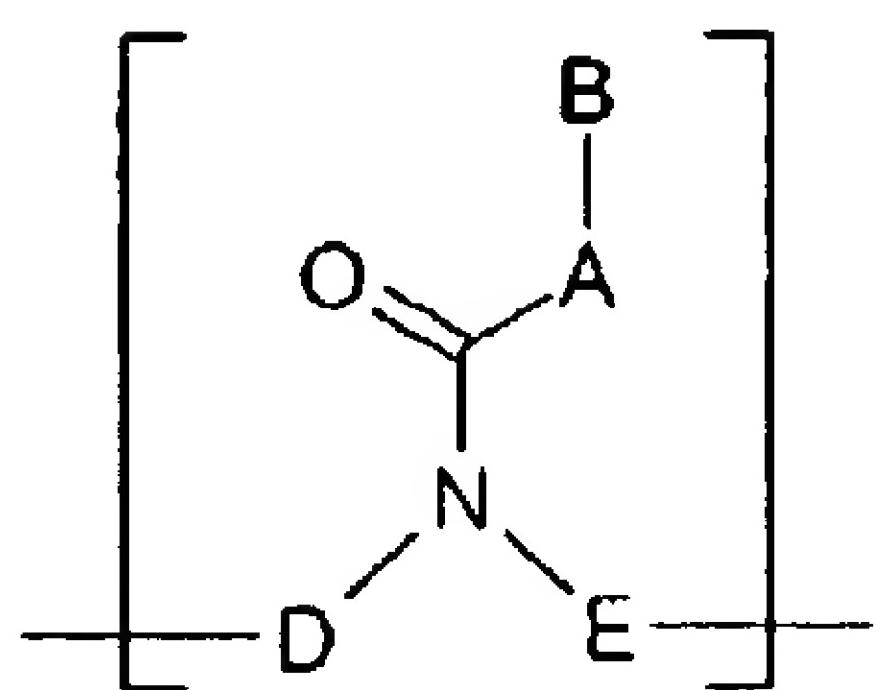
$\text{R}_7$  and  $\text{R}_8$  are, independently of each other, C<sub>1</sub>-C<sub>18</sub>-alkyl or hydroxy-C<sub>1</sub>-C<sub>18</sub>-alkyl.

and wherein {POLY} is described by Formula II



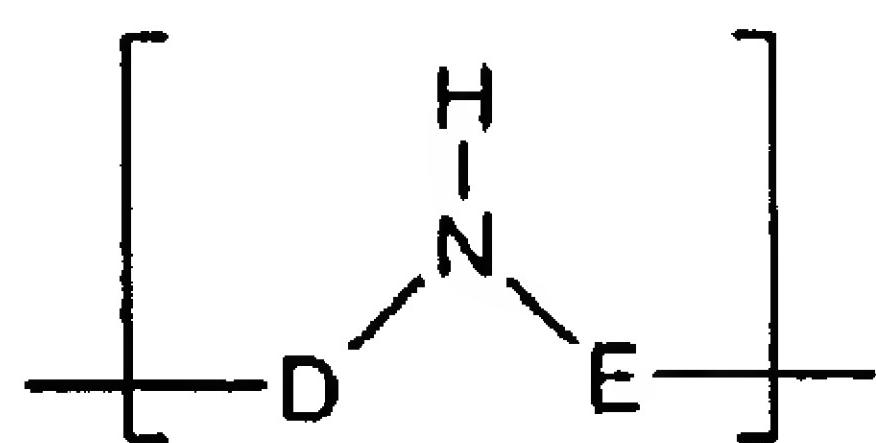
Formula II,

wherein {BLOCK} is, independently of any other {BLOCK}, described by Formula IIIA,



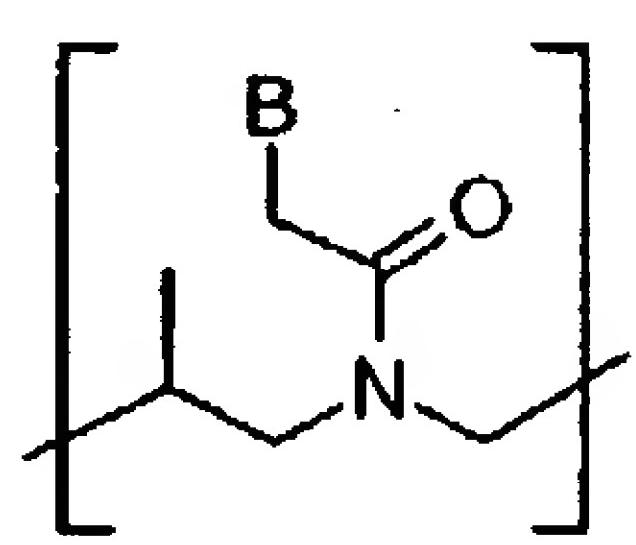
Formula IIIA

Formula IIIB,

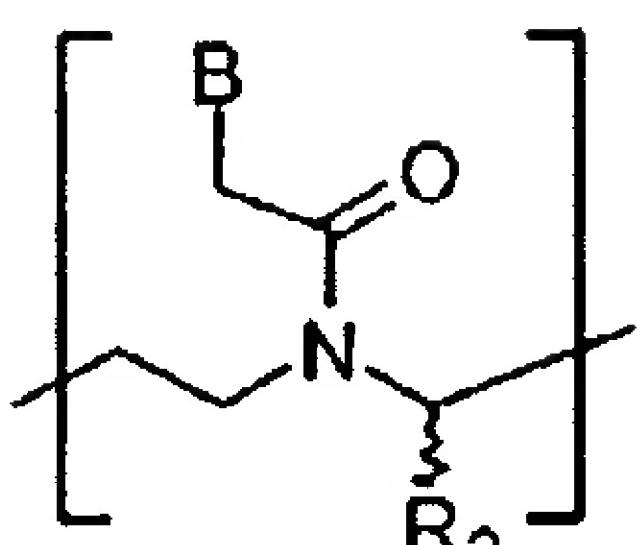


Formula IIIB

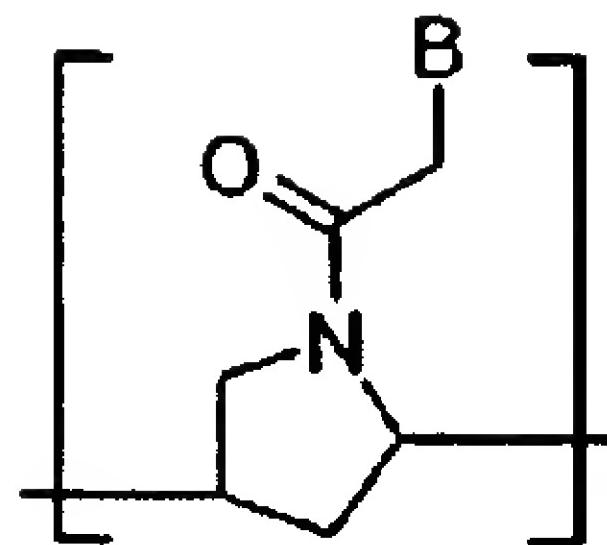
or Formulae IV A to IV G,



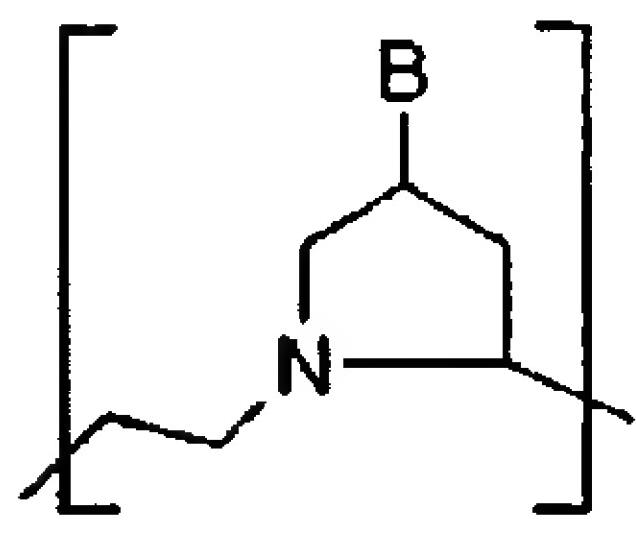
Formula IV A



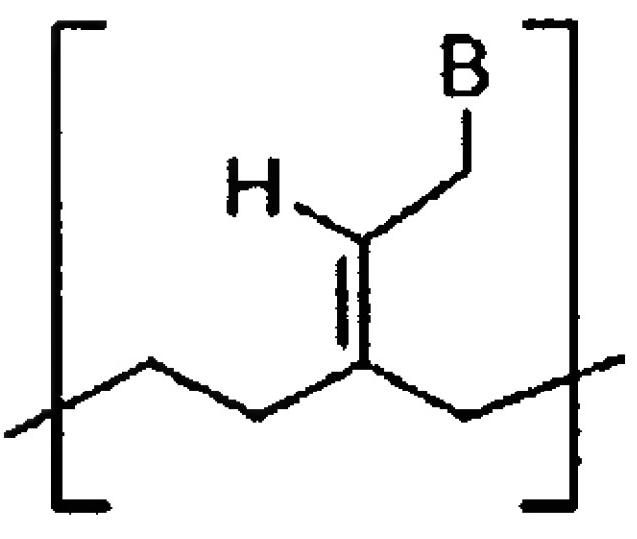
Formula IV B



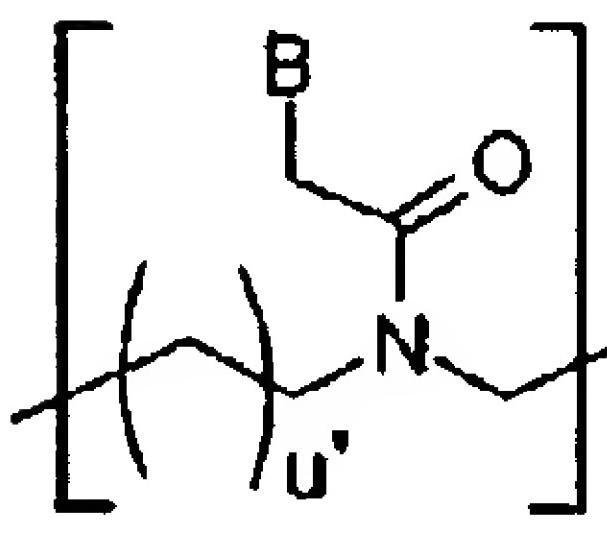
Formula IV C



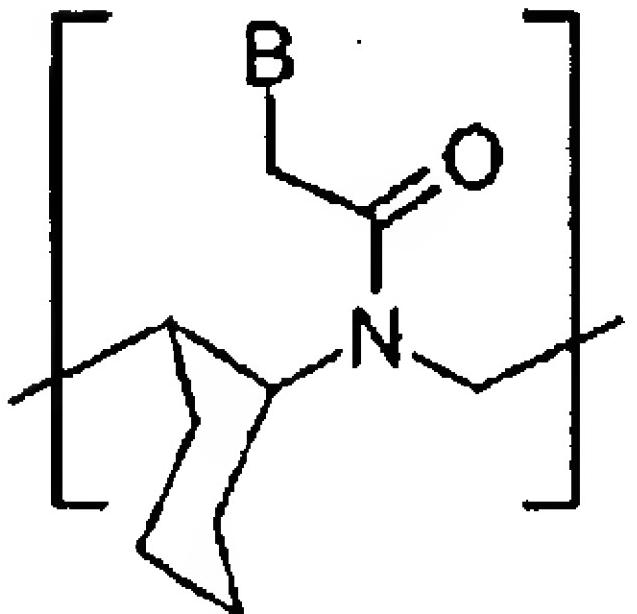
Formula IV D



Formula IV E



Formula IV F



Formula IV G

wherein each building block {BLOCK} can be different,

and wherein

**z'** is from 0 to 100;

**A** is, independently of any other A,  $(CR_1R_2)_s$ , wherein s is from 1 to 3;

**B** is, independently of any other B,  
an aromatic radical which optionally possesses heteroaromatic character,  
hydrogen,

hydroxyl,  
 $C_1\text{-}C_{18}\text{-alkyl}$ ,  
or a nucleobase or its prodrug form,  
wherein at least one B radical is a nucleobase;

D is, independently of any other D,  $(CR_3R_4)_t$ , wherein t is from 2 to 10,  
wherein two adjacent  $R_3$  and  $R_4$  radicals can form a  $C_5\text{-}C_8\text{-cycloalkyl}$   
ring;

E is, independently of any other E,  $(CR_5R_6)_{u'}$ ,

$R_5$  and  $R_6$  are, independently of each other, a radical consisting of hydrogen  
or  $C_1\text{-}C_6\text{-alkyl}$ , or an amino acid side chain, wherein two adjacent  
 $R_5$  and  $R_6$  radicals can form a  $C_5\text{-}C_8\text{-cycloalkyl}$  ring or a spiro  
compound, and

wherein  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ , and  $u'$  are as defined above;

and physiologically tolerated salts of the PNA derivative of the Formula I,

with the proviso that at least one Y or Z radical is hydroxyl, mercapto, oxyanion,  
or thioate.

2. A PNA derivative as claimed in claim 1, wherein at least one Y or Z radical in Formula I is oxyanion or thioate in a pH range from 4.5 to 14.
3. A PNA derivative as claimed in claim 1, wherein D is (CH<sub>2</sub>)<sub>2</sub>.
4. A PNA derivative as claimed in claim 1, wherein A and E are CH<sub>2</sub>.
5. A PNA derivative as claimed in claim 1, wherein Q is a hydroxyaminoalkyl radical or a carrier sequence.
6. A PNA derivative as claimed in claim 1, wherein B is, independently of any other B, adenine, cytosine, 5-methylcytosine, guanine, thymine, uracil, purine, 2,6-diaminopurine, N<sup>4</sup>N<sup>4</sup>-ethanocytosine, N<sup>6</sup>N<sup>6</sup>-ethano-2,6-diaminopurine, 5-(C<sub>3</sub>-C<sub>6</sub>)-alkynyluracil, 5-(C<sub>3</sub>-C<sub>6</sub>)-alkynylcytosine, 5-(1-propargylamino)uracil, 5-(1-propargylamino)cytosine, phenoxazine, 9-aminoethoxyphenoxazine, 5-fluorouracil or pseudouracil, 5-(hydroxymethyl)uracil, 5-aminouracil, pseudouracil, dihydrouracil, 5-(C<sub>1</sub>-C<sub>6</sub>)-alkyluracil, 5-(C<sub>1</sub>-C<sub>6</sub>)-alkylcytosine, 5-(C<sub>2</sub>-C<sub>6</sub>)-alkenylcytosine, 5-fluorocytosine, 5-chlorouracil, 5-chlorocytosine, 5-bromouracil, 5-bromocytosine, 7-deazaadenine, 7-deazaguanine, 8-azapurine, or a 7-deaza-7-substituted purine.
7. A PNA derivative as claimed in claim 1, wherein W is oxygen and Y is hydroxyl or oxyanion.

8. A PNA derivative as claimed in claim 1, wherein X is U-(C<sub>2</sub>-C<sub>22</sub>-alkanediyl)-U or U-(CH<sub>2</sub>CH<sub>2</sub>-O)<sub>u</sub>.
9. A PNA derivative as claimed in claim 1, wherein Z is a phosphate, a C<sub>1</sub>-to C<sub>22</sub>-radical, a C<sub>1</sub>-C<sub>22</sub>-U radical, hydroxy-C<sub>1</sub>-C<sub>18</sub>-U, an aminoalkyl-U radical, a group of the Formula R<sub>9</sub>-(CH<sub>2</sub>CH<sub>2</sub>-O)<sub>m</sub>, or a mercaptoalkyl-U radical.
10. A PNA derivative as claimed in claim 1, wherein X and Z are, independently of each other, biotin, fluorescein, or lexitropsin, or derivatives thereof.
11. A PNA derivative as claimed in claim 1, wherein X and Z are, independently of each other, rhodamine, TAMRA, or cyanine dye.
12. A PNA derivative as claimed in claim 1, wherein X and Z are, independently of each other, Dabcyl, psoralen, acridine, DNP, or cholesterol.
13. A PNA derivative as claimed in claim 1, wherein {POLY} comprises a nucleotide base sequence that binds to at least one sequence of at least one tumor suppressor gene, oncogene, or telomerase, or to their mRNA transcription products.

14. A PNA derivative as claimed in claim 13, wherein the base sequence of the PNA moiety is directed against the translation start of HA-ras mRNA.
15. A pharmaceutical comprising the PNA derivative as claimed in claim 1 and a physiologically acceptable carrier or excipient.
16. A process for detecting a nucleic acid of interest, said process comprising
  - labeling a PNA derivative as claimed in claim 1 with a detectable label, wherein the PNA derivative comprises a base sequence that specifically hybridizes with at least one sequence present in the nucleic acid of interest under selected conditions,
  - combining said labeled PNA derivative with a sample suspected of containing the nucleic acid of interest, and
  - detecting specific binding of said labeled PNA derivative to said nucleic acid of interest,wherein specific binding indicates the presence of the nucleic acid of interest in the sample.

17. The process as claimed in claim 16, wherein the process is fluorescence in-situ hybridization (FISH).
18. The process as claimed in claim 17, wherein the nucleic acid of interest is a nucleic acid of a microorganism or virus.
19. The process of claim 17, wherein the process further comprises quantifying the detected nucleic acids.
20. The PNA derivative as claimed in claim 1, wherein the PNA derivative is an antisense agent, anti-gene agent, decoy agent, or chimeroplast agent.
21. The PNA derivative as claimed in claim 1, wherein the PNA derivative is a detection reagent.
22. A PNA chip comprising a PNA derivative as claimed in claim 1 and a substrate suitable as a solid support for fabricating a microarray.
23. A biosensor comprising a PNA derivative as claimed in claim 1 and a substrate suitable for conducting a signal from the PNA derivative to a detection device.

31. A PNA derivative as claimed in claim 1, wherein u' is from 1 to 4.
32. A PNA derivative as claimed in claim 1, wherein u' is 1.
33. A PNA derivative as claimed in claim 1, wherein R<sub>1</sub> and R<sub>2</sub> are both hydrogen.
34. A PNA derivative as claimed in claim 1, wherein R<sub>3</sub> and R<sub>4</sub> are both hydrogen.
35. A PNA derivative as claimed in claim 1, wherein X is a bifunctional labeling group, and wherein X is fluorescein, rhodamine, TAMRA, biotin or a biotin derivative, pyrene, dinitrophenyl, acridine, cyanine dye, Dabcyl, digoxigenin, or an Edans derivative.
36. A PNA derivative as claimed in claim 35, wherein the bifunctional labeling group is a biotin derivative.

37. A PNA derivative as claimed in claim 1, wherein X is a bifunctional group for crosslinking with complementary nucleic acids.
38. A PNA derivative as claimed in claim 37, wherein X is a psoralen derivative.
39. A PNA derivative as claimed in claim 1, wherein X is a bifunctional group which promotes intracellular uptake.
40. A PNA derivative as claimed in claim 39, wherein X is cholesteryl, adamantyl, or a vitamin E derivative.

41. A PNA derivative as claimed in claim 1, wherein X is a bifunctional group which increases the binding affinity of the PNA derivative for a target nucleic acid.
42. A PNA derivative as claimed in claim 41, wherein X is acridine or a lexitropsin derivative.
43. A PNA derivative as claimed in claim 1, wherein m is from 2 to 10.
44. A PNA derivative as claimed in claim 1, wherein z is a monofunctional or bifunctional labeling group.
45. A PNA derivative as claimed in claim 44, wherein z is fluorescein, rhodamine, TAMRA, biotin or a biotin derivative, pyrene, dinitrophenyl, acridine, cyanine dye, Dabcyl, digoxigenin, or an Edans derivative.
46. A PNA derivative as claimed in claim 45, wherein z is a biotin derivative.
47. A PNA derivative as claimed in claim 1, wherein z is a monofunctional or bifunctional crosslinking group.
48. A PNA derivative as claimed in claim 1, wherein z is a psoralen derivative.
49. A PNA derivative as claimed in claim 1, wherein z is a monofunctional or bifunctional group which promotes intracellular uptake.
50. A PNA derivative as claimed in claim 49, wherein z is cholestryl, adamantyl, or a vitamin E derivative.

51. A PNA derivative as claimed in claim 1, wherein z is a monofunctional or bifunctional group which promotes the binding affinity of the PNA derivative for a target nucleic acid.
52. A PNA derivative as claimed in claim 51, wherein z is a lexitropsin derivative.
53. A PNA derivative as claimed in claim 1, wherein n is from 0 to 10.
54. A PNA derivative as claimed in claim 1, wherein n is from 0 to 3.
55. A PNA derivative as claimed in claim 1, wherein z' is from 0 to 100.
56. A PNA derivative as claimed in claim 1, wherein z' is from 1-20.
57. A PNA derivative as claimed in claim 1, wherein z' is from 4-15.

58. A PNA derivative as claimed in claim 1, wherein s is 1.
59. A PNA derivative as claimed in claim 1, wherein B is, independently of any other B, a nucleobase which occurs naturally.
60. A PNA derivative as claimed in claim 1, wherein B is, independently of any other B, a nucleobase which does not occur naturally.
61. A PNA derivative as claimed in claim 1, wherein t is from 2 to 10.
62. A PNA derivative as claimed in claim 1, wherein t is from 2 to 4.
63. A PNA derivative as claimed in claim 1, wherein t is 2.
64. A PNA derivative as claimed in claim 1, wherein two adjacent R<sub>3</sub> and R<sub>4</sub> radicals form a C<sub>5</sub>-C<sub>8</sub>-cycloalkyl ring.
65. A PNA derivative as claimed in claim 1, wherein R<sub>5</sub> and R<sub>6</sub> are both hydrogen.
66. A PNA derivative as claimed in claim 1, wherein at least one Y or Z radical in Formula I is oxyanion or thioate in a pH range from 6.5 to 12.
67. A PNA derivative as claimed in claim 1, wherein at least one Y or Z radical in Formula I is oxyanion or thiolate in a pH range from 6.5 to 9.
68. A PNA derivative as claimed in claim 5, wherein Q is a hydroxyaminohexyl radical.

69. A PNA derivative as claimed in claim 5, wherein Q is transportan, insulin-like growth factor, a nuclear localization signal, or an affinity tag.
70. A PNA derivative as claimed in claim 69, wherein Q is a (His)<sub>6</sub> chain affinity tag.
71. A PNA derivative as claimed in claim 8, wherein X is O-(C<sub>2</sub>-C<sub>22</sub>-alkanediy)-O.
72. A PNA derivative as claimed in claim 8, wherein X is O-(CH<sub>2</sub>)<sub>2-6</sub>O.
73. A PNA derivative as claimed in claim 8, wherein X is O-(CH<sub>2</sub>CH<sub>2</sub>-O)<sub>u</sub>, wherein u' is from 1 to 6.

74. A PNA derivative as claimed in claim 9, wherein Z is a C<sub>1</sub>-C<sub>22</sub>-alkoxy radical.
75. A PNA derivative as claimed in claim 9, wherein Z is C<sub>16</sub>-alkoxy.
76. A PNA derivative as claimed in claim 9, wherein Z is hydroxy-C<sub>1</sub>-C<sub>18</sub>-O.
77. A PNA derivative as claimed in claim 9, wherein Z is HO-(CH<sub>2</sub>)<sub>3-12</sub>O.
78. A PNA derivative as claimed in claim 9, wherein Z is an aminoalkoxy radical.
79. A PNA derivative as claimed in claim 9, wherein Z is 6-aminohexoxy or 5-aminopentoxy.
80. A PNA derivative as claimed in claim 9, wherein R<sub>9</sub> is OH or NH<sub>2</sub> and m is from 1 to 6.
81. A PNA derivative as claimed in claim 9, wherein Z is HO(CH<sub>2</sub>CH<sub>2</sub>-O)<sub>2</sub>.
82. A PNA derivative as claimed in claim 9, wherein Z is HO(CH<sub>2</sub>CH<sub>2</sub>-O)<sub>6</sub>.
83. A PNA derivative as claimed in claim 9, wherein Z is H<sub>2</sub>N-(CH<sub>2</sub>CH<sub>2</sub>-O)<sub>2</sub>.
84. A PNA derivative as claimed in claim 9, wherein Z is a mercaptoalkoxy radical.

85. A PNA derivative as claimed in claim 9, wherein Z is 6-mercaptophexyloxy.